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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,150	02/17/2004	David Munn	NEWL-005/02US 142996-2008	1273

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EXAMINER	
THOMAS, TIMOTHY P	

ART UNIT	PAPER NUMBER
1628	

MAIL DATE	DELIVERY MODE
12/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/780,150	MUNN ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,98-101,103,105,106,108,124-127,129 and 131-133* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,2,5-7,10,17,18,20-24,26,27,43,97-103,105,106,108-129 and 131-133.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 1,5-7,10,17,18,20-24,26,27,43,97,102,109-123 and 128.

DETAILED ACTION

Election/Restrictions

1. This application contains claims 1, 5-7, 10, 17-18, 20-24, 26-27, 43, 97, 102, 109-123, 128, drawn to an invention nonelected with traverse in the replies filed on 3/23/2009 and 12/19/2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Arguments

2. Applicants' arguments, filed 9/14/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

3. Applicant's arguments with respect to the rejection under 35 USC 102 have been fully considered but they are not persuasive:

Claims 2, 98-101, 103, 105-106 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Den Eynde et al. (WO 00/66764; 2000; cited in prior Office Action).

The rejection is maintained for the reasons of record.

Applicant argues that Van Den Eynde teaches 1-methyl-DL-tryptophan and NOT compositions "consisting essentially of 1-methyl-D-tryptophan" required by the instant claims; that the instant specification states "the [D] isomer of 1 MT was found to be effective at one quarter of the dose used for the racemic preparation, which makes clear

that the presence of the L isomer in the racemic mixture materially affects the basic and novel characteristics of the invention. The referenced passage is in the disclosure of the effect of 1MT on established tumors, and synergy with radiation or cyclophosphamide, and references Figure 11D. A review of the figure demonstrates that 1-[D]-MT alone (without cyclophosphamide) has no effect on the progress of tumor growth. This does not demonstrate that the [D] isomer alone has any effect on the cell line; only in the presence of another agent was the synergistic result observed. A review of the claims indicates that claim 2 recites "consisting essentially of 1-methyl-D-tryptophan" language; however, claim 108, which further limits claim 2, specifically recites the only limitation is that the pharmaceutical composition does not contain 1-methyl-L-tryptophan. Therefore, the language "consisting essentially of 1-methyl-D-tryptophan" is inconsistent with the argument that the meaning of "consisting essentially of" excludes the L isomer.

It is also clear that the presence of cyclophosphamide administered in combination with 1-methyl-D-tryptophan does materially affect the basic and novel characteristic of the invention; Figure 11 D clearly demonstrates a reduction in tumor area for this combination, which is synergistic over the effect expected for both compounds administered separately. "Consisting essentially of" would therefore properly be construed to exclude cyclophosphamide. In contrast to this, withdrawn claim 7 specifically recites that cyclophosphamide would be present, an embodiment within the scope of claim 2 also.

Both of the above fact patterns make clear that the specification, when taken together with the claims, is confusing as to what is meant by the phrase "consisting essentially of". As previously discussed in the record, MPEP 2105 indicates that, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising". Accordingly, the language of the instant claims is ineffective to exclude 1-methyl-L-tryptophan from being administered, and Van Den Eynde anticipates the instant claims.

It is noted that the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention has been shifted to applicant. (In the instant case, applicant would have the burden to show that the presence of 1-methyl-L-tryptophan will change the progression of a tumor growth or timing of a relapse of tumor growth, in a tumor, such as the elected melanoma tumor.) This burden has not been met.

4. Applicant's arguments with respect to the enablement rejection have been fully considered but they are not persuasive:

Claims 2, 98-101, 103, 105-106, 108, 124-127, 129 and 131-133 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for delaying the progression of a melanoma tumor comprising administering the combination of 1-methyl-D-tryptophan and cyclophosphamide, does not reasonably provide enablement for delaying the relapse of or progression of a melanoma tumor or

any other tumor by administering 1-methyl-D-tryptophan without an additional chemotherapeutic agent.

The rejection of Claims 2, 98-101, 103, 105-106, 108, 124-127, 129 and 131-132 is maintained for the reasons of record. The rejection is extended to claim 133 for the reasons of record, which is necessitated by the amendment adding this claim.

Applicant argues that the Declaration of Dr. Mario Mautino clearly shows the efficacy of 1-methyl-D-tryptophan in the absence of an additional chemotherapeutic agent based on an experiment conducted by Dr. Mautino and his discussion of an article by Hou et al. submitted with the Declaration. A review of the data indicates that the experiment conducted by Dr. Mautino demonstrates that in a single lung cancer line, LLC, mice implanted with these tumors had a few days extended lifespan compared to control animals. The declaration does not state whether this tumor line is an IDO expressing cell line, but based on the instant disclosure, it is assumed this is the case. This data demonstrates extended lifespan, which may be construed to support a delay in the progression of this specific cell line.

A review of the Hou article at Figure 5C demonstrates a delay in the progression of the single melanoma cell line that has a large expression of IDO, supporting a delay in the progression of an IDO-expressing melanoma cell line.

It is noted that neither of these data sources support the alternative claim to delaying the relapse of any tumor, including lung and melanoma lines reported on. No do the data support the broad extensive generic claim to delaying the progression of **every** tumor, whether or not the tumor expresses IDO, even the subject matter under

examination of melanoma tumors are not supported for every. Applicant is advised that a claim limited to a method of delaying the progression of an IDO-expressing melanoma or lung tumor when 1-methyl-D-tryptophan is administered without an additional chemotherapeutic agent present would be considered enabled. This subject matter would be commensurate in scope with the data presented. The enablement rejection is maintained for embodiments outside of the scope of this limited subject matter.

5. Applicant's arguments with respect to the rejection under 35 USC 112, 2nd paragraph have been fully considered but they are not persuasive:

Claims 2, 98-101, 103, 105-106, 108, 124-127, 129 and 131-133 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection is maintained for claims 2, 98-101, 103, 105-106, 108, 124-127, 129 and 131-132 for the reasons of record. The rejection of record is also applicable to claim 133; the extension to claim 133 is necessitated by the claim amendment adding this claim.

Additionally, claim 133 is confusing with respect to the language "is substantially free of 1-methyl-L-tryptophan". It is not clear what level of 1-methyl-L-tryptophan is permitted in this method by substantially free. Substantially has the meaning of being largely but not wholly that which is specified; it appears that this language requires a small amount of the L-isomer is actually present in the method by the meaning "largely but not wholly free" of the L-isomer. It is not clear whether some L-isomer is required or

whether all L-isomer may be absent. It is also not clear at what level the upper amount of L-isomer is cutoff. The "largely free" upper limit is taken to mean that a smaller amount of L-isomer is required than the D-isomer (e.g., up to 49.9% of the L-isomer may be present). (The Van Den Eynde teaching of the DL racemic mixture would not read on the claim when so construed; therefore, this claim is not included in the rejection under 35 USC 102.)

It is noted that applicant has not separately addressed this rejection, except for the comments related to this subject that were made under the heading of the rejection under 35 USC 102. These arguments have been addressed above.

Conclusion

6. No claim is allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1628

/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642